Remarks

This is in response to the Official Action of July 26, 2002. The points raised therein are addressed below in the order originally set forth.

Claims 1-16 stand rejected as indefinite under the second paragraph of 35 USC 112, the Examiner noting that claims 1 and 6 lack sufficient antecedent basis for "said subject". The claims have been amended as suggested by the Examiner, and it is respectfully submitted that this rejection may now be withdrawn.

Claims 1-16 stand rejected as lacking enablement under the first paragraph of 35 USC 112. For the reasons set forth below, it is respectfully submitted that this rejection should be withdrawn.

As an initial matter, it is noted that the present inventor's findings on the relationship of the serotonin transporter promoter long allele to stress as an indication of disease risk is accepted in the research community. *See, e.g.,* F. Fumeron et al., *Serotonin Transporter Gene Polymorphism and Myocardial Infarction,* Circulation **105**, 2943-45 (2002)(copy enclosed)(citing the present inventor at note 11 therein). Applicant also notes S. Everson et al., *Stress-induced blood pressure reactivity and incident stroke in middle-aged men,* Stroke **32**, 1263-1270 (2001)(a copy of which will be provided if the Examiner so desires). These publications indicate the ready applicability of the invention by skilled persons.

With respect to the Examiner's applicability of the *Wands* factors to the instant invention, reconsideration is respectfully requested. For *Nature of the Invention,* please note that the invention is concerned with screening methods rather than therapeutic treatments, with the former historically receiving much less scrutiny for enablement than the latter. For *Presence or Absence of Working Examples,* note that working examples are not considered a mandatory aspect of disclosure. For *Amount of Direction and Guidance,* note that the stress response has been exhaustively studied and is well known, the long allele of the serotonin transporter is known, and that determining whether a subject is both subjected to a stress response and carries the long allele can be carried out with routine skill. For *level of predictability and unpredictability in the art,* note that it is the steps required by the claims and not the linkage recited by the claims which should be the focus of this inquiry, and the steps required by the claims can be routinely carried out as noted above. Finally, for

quantity of experimentation necessary, it is submitted that, since the stress response is known and the long allele is known, little if any experimentation is required to implement the claims. Note that the claims do not require the absolute prediction of disease, but only "increased risk" of disease. This case is nothing like *Genentech,* cited in the action, where the claims sought to encompass numerous unknown compounds based on a disclosure of a particular compound. Accordingly, it is respectfully submitted that this rejection should be withdrawn.

Claims 1 and 2 stand rejected as anticipated under 35 USC 102(b) by Arinami et al. This rejection is respectfully traversed. In applying Arinami et al., the Examiner notes that "[s]ince the claims do not make clear what type of stress is encompassed by the claims, the term 'stress' has been broadly interpreted to include stress due to smoking." However, the invention is not concerned with the damaging effects of administering a carcinogen to the subject, but is instead concerned with "stimulus that induces a physiological stress response in a subject" (specification, page 4, claim 29-30). Clearly smoking does not meet this definition of stress because to a smoker it is the cessation of smoking, not the act of smoking itself, which is stressful. To clarify the issues, the definition of stress found in the specification has been inserted into claim 1. In view of this clarification, it is respectfully submitted that this rejection should be withdrawn.

The changes made to the claims by this amendment are shown in the attached **"Version with Markings to Show Changes Made."**

It is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,

Kenneth D. Sibley
Registration No. 31,665

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec
Post Office Box 37428
Raleigh, North Carolina 27627
Telephone (919) 854-1400
Facsimile (919) 854-1401
Enclosure: F. Fumeron et al.

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, Washington, DC 20231, on October 28, 2002.

Vickie Diane Prior
Date of Signature: October 28, 2002

Version with Markings to Show Changes Made

1 (amended). A method of screening human subjects for increased risk of disease in response to stimulus that induces a physiological stress response in said subject, said method comprising:

determining the presence of at least one serotonin transporter gene promoter long allele in a human subject;

the presence of at least one long allele serotonin transporter gene promoter genotype indicating that said human subject is at increased risk of disease in response to stress.

6 (amended). A method of screening human subjects for increased risk of infectious disease, said method comprising:

determining the presence of at least one serotonin transporter gene promoter long allele in a human subject;

the presence of at least one long allele serotonin transporter gene promoter genotype indicating that said human subject is at increased risk of infectious disease.